Analyses of regenerative wave patterns in adult hair follicle populations reveal macro-environmental regulation of stem cell activity.

Journal: Int J Dev Biol

Publication Year: 2009

Authors: Maksim V Plikus, Randall B Widelitz, Rob Maxson, Cheng-Ming Chuong

PubMed link: 19378257

Funding Grants: CIRM Stem Cell Biology Training Grant

Public Summary:

Scientific Abstract:
The control of hair growth in the adult mammalian coat is a fascinating topic which has just begun to be explored with molecular genetic tools. Complex hair cycle domains and regenerative hair waves are present in normal adult (> 2 month) mice, but more apparent in mutants with cyclic alopecia phenotypes. Each hair cycle domain consists of initiation site(s), a propagating wave and boundaries. By analyzing the dynamics of hair growth, time required for regeneration after plucking, in situ hybridization and reporter activity, we showed that there is oscillation of intra-follicular Wnt signaling which is synchronous with hair cycling, and there is oscillation of dermal bone morphogenetic protein (BMP) signaling which is asynchronous with hair cycling. The interactions of these two rhythms lead to the recognition of refractory and competent phases in the telogen, and autonomous and propagating phases in the anagen. Boundaries form when propagating anagen waves reach follicles which are in refractory telogen. Experiments showed that Krt14-Nog mice have shortened refractory telogen and simplified wave dynamics. Krt14-Nog skin grafts exhibit non-autonomous interactions with surrounding host skin. Implantation of BMP coated beads into competent telogen skin prevents hair wave propagation around the bead. Thus, we have developed a new molecular understanding of the classic early concepts of inhibitory "chalone", suggesting that stem cells within the hair follicle micro-environment, or other organs, are subject to a higher level of macro-environmental regulation. Such a novel understanding has important implications in the field of regenerative medicine. The unexpected links with Bmp2 expression in subcutaneous adipocytes has implications for systems biology and Evo-Devo.